Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1635jxs

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	JUL 20	Powerful new interactive analysis and visualization software, STN AnaVist, now available
NEWS 4	AUG 11	STN AnaVist workshops to be held in North America
NEWS 5	AUG 30	CA/CAplus -Increased access to 19th century research documents
NEWS 6	AUG 30	CASREACT - Enhanced with displayable reaction conditions
NEWS 7	SEP 09	ACD predicted properties enhanced in REGISTRY/ZREGISTRY
NEWS 8	OCT 03	MATHDI removed from STN
NEWS 9	OCT 04	CA/CAplus-Canadian Intellectual Property Office (CIPO) added to core patent offices
NEWS 10	OCT 06	STN AnaVist workshops to be held in North America
NEWS 11	OCT 13	New CAS Information Use Policies Effective October 17, 2005
NEWS 12	OCT 17	STN(R) AnaVist(TM), Version 1.01, allows the export/download of CAplus documents for use in third-party analysis and visualization tools
NEWS 13	OCT 27	Free KWIC format extended in full-text databases
NEWS 14	OCT 27	DIOGENES content streamlined
NEWS 15	OCT 27	EPFULL enhanced with additional content

NEWS EXPRESS	JUNE 13 CURRENT WINDOWS VERSION IS V8.0, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 18:57:51 ON 13 NOV 2005

=> s antisense or anti-sense or (complem? (2n) (oligonucl? or nucle?))
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an

```
index.  Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of
commands which can be used in this file.

=> FIL MEDLINE BIOSIS SCISEARCH EMBASE CA
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       2.10       2.10

FILE 'MEDLINE' ENTERED AT 19:03:54 ON 13 NOV 2005

FILE 'BIOSIS' ENTERED AT 19:03:54 ON 13 NOV 2005
Copyright (c) 2005 The Thomson Corporation

FILE 'SCISEARCH' ENTERED AT 19:03:54 ON 13 NOV 2005
Copyright (c) 2005 The Thomson Corporation

FILE 'EMBASE' ENTERED AT 19:03:54 ON 13 NOV 2005
Copyright (c) 2005 Elsevier B.V. All rights reserved.

FILE 'CA' ENTERED AT 19:03:54 ON 13 NOV 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

=> s antisense or anti-sense or (complem? (2n) (oligonucl? or nucle?))
L1      157727 ANTISENSE OR ANTI-SENSE OR (COMPLEM? (2N) (OLIGONUCL? OR NUCLE?)
               )

=> s creb?
L2       26280 CREB?

=> s l1 (w) l2
L3          19 L1 (W) L2

=> s l1 (p) l2
L4         472 L1 (P) L2

=> s l1 (s) l2
L5         247 L1 (S) L2

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6           90 DUP REM L5 (157 DUPLICATES REMOVED)

=> s l6 and py<=2001
   4 FILES SEARCHED...
L7          58 L6 AND PY<=2001

=> s l7 and creb
L8          57 L7 AND CREB

=> s l7 and (l1 (s) l2)
L9          58 L7 AND (L1 (S) L2)

=> s l8 and (l1 (5n) l2)
L10         46 L8 AND (L1 (5N) L2)

=> d l10 ibib abs 1-46

L10  ANSWER 1 OF 46     MEDLINE on STN
ACCESSION NUMBER:   2001692149     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 11739600
TITLE:              cAMP response element-binding protein is required for
```

dopamine-dependent gene expression in the intact but not the dopamine-denervated striatum.

AUTHOR: Andersson M; Konradi C; Cenci M A

CORPORATE SOURCE: Department of Physiological Sciences, Neurobiology Division, Lund University, Wallenberg Neuroscience Centre, 221 84 Lund, Sweden.

SOURCE: Journal of neuroscience : official journal of the Society for Neuroscience, **(2001 Dec 15)** 21 (24) 9930-43.
Journal code: 8102140. ISSN: 1529-2401.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200201

ENTRY DATE: Entered STN: 20011213
Last Updated on STN: 20020128
Entered Medline: 20020123

AB The cAMP response element-binding protein (**CREB**) is believed to play a pivotal role in dopamine (DA) receptor-mediated nuclear signaling and neuroplasticity. Here we demonstrate that the significance of **CREB** for gene expression depends on the experimental paradigm. We compared the role of **CREB** in two different but related models: l-DOPA administration to unilaterally 6-hydroxydopamine lesioned rats, and cocaine administration to neurologically intact animals. **Antisense** technology was used to produce a local knockdown of **CREB** in the lateral caudate-putamen, a region that mediates the dyskinetic or stereotypic manifestations associated with l-DOPA or cocaine treatment, respectively. In intact rats, **CREB antisense** reduced both basal and cocaine-induced expression of c-Fos, FosB/DeltaFosB, and prodynorphin mRNA. In the DA-denervated striatum, **CREB** was not required for l-DOPA to induce these gene products, nor did **CREB** contribute considerably to DNA binding activity at cAMP responsive elements (CREs) and CRE-like enhancers. DeltaFosB-related proteins and JunD were the main contributors to both CRE and AP-1 DNA-protein complexes in l-DOPA-treated animals. In behavioral studies, intrastriatal **CREB** knockdown caused enhanced activity scores in intact control animals and exacerbated the dyskinetic effects of acute l-DOPA treatment in 6-OHDA-lesioned animals. These data demonstrate that **CREB** is not required for the development of l-DOPA-induced dyskinesia in hemiparkinsonian rats. Moreover, our results reveal an unexpected alteration of nuclear signaling mechanisms in the parkinsonian striatum treated with l-DOPA, where AP-1 transcription factors appear to supersede **CREB** in the activation of CRE-containing genes.

L10 ANSWER 2 OF 46 MEDLINE on STN

ACCESSION NUMBER: 2001550783 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11599000

TITLE: Effect of cyclic AMP on the expression of myelin basic protein species and myelin proteolipid protein in committed oligodendrocytes: differential involvement of the transcription factor **CREB**.

AUTHOR: Afshari F S; Chu A K; Sato-Bigbee C

CORPORATE SOURCE: Department of Biochemistry and Molecular Biophysics, Medical College of Virginia Campus, Virginia Commonwealth University, Richmond, Virginia 23298-0614, USA.

CONTRACT NUMBER: NS35097 (NINDS)

SOURCE: Journal of neuroscience research, **(2001 Oct 1)** 66 (1) 37-45.
Journal code: 7600111. ISSN: 0360-4012.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011015
Last Updated on STN: 20020122
Entered Medline: 20011204

AB Our previous results support the idea that **CREB** (cyclic AMP-response element binding protein) may be a mediator of neuroligand and growth factor signals that, coupled to different signal transduction pathways, play different roles at specific stages of oligodendrocyte development. In the early stages, when cells are immature precursors, **CREB** may play a role as a mediator of protein kinase C (PKC)/mitogen-activated protein kinase (MAPK) pathways regulating cell proliferation. In contrast, at a later stage, when cells are already committed oligodendrocytes, **CREB** seems to play an important role as a mediator in the stimulation of myelin basic protein (MBP) expression by cyclic AMP (cAMP). In this study, we have investigated whether cAMP and **CREB** play a role in regulating the expression of all or on the other hand particular MBP isoforms. The results indicated that treatment of committed oligodendrocytes with the cAMP analogue db-cAMP results in a pattern of expression of MBP-related polypeptides that most closely resembles the pattern of MBPs observed in cerebra from adult animals. Experiments in which **CREB** expression was inhibited using a **CREB antisense** oligonucleotide, suggested that **CREB** is involved in the cAMP-dependent stimulation of all the MBP isoforms. In contrast, we have found that db-cAMP stimulates the expression of myelin proteolipid protein (PLP) in a process that occurs despite inhibition of **CREB** expression. These results support the idea that cAMP stimulates the maturation of oligodendrocytes and stress the fact multiple mechanisms may convey the action of this second messenger modulating oligodendrocyte differentiation and myelination.

L10 ANSWER 3 OF 46 MEDLINE on STN
ACCESSION NUMBER: 2001234816 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11021976
TITLE: Antagonism of NPY-induced feeding by pretreatment with cyclic AMP response element binding protein antisense oligonucleotide.
AUTHOR: Chance W T; Sheriff S; Peng F; Balasubramaniam A
CORPORATE SOURCE: Medical Research Service, VA Medical Center, 3200 Vine Street, Cincinnati, OH 45220, USA.
CONTRACT NUMBER: DK 53548 (NIDDK)
GM 47122 (NIGMS)
SOURCE: Neuropeptides, **(2000 Jun-Aug)** 34 (3-4) 167-72.
Journal code: 8103156. ISSN: 0143-4179.
PUB. COUNTRY: Scotland: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010517
Last Updated on STN: 20010517
Entered Medline: 20010503

AB Although second messenger systems subserving neuropeptide Y (NPY)-mediated behaviors have been identified for a variety of receptors in several tissues, downstream signaling events are not well known. The nuclear binding protein, cyclic AMP response element binding protein (**CREB**) appears to be a transcription factor that is activated following injection of NPY into rat hypothalamus. To allow determination of the functional nature of **CREB** mediation of NPY-induced feeding, injection cannulae were implanted into the perifornical hypothalamus of 18 rats. Treatment of seven rats with **CREB antisense** oligonucleotide (15 ug) significantly antagonized NPY feeding for up to one week after treatment, while similar injections of **CREB** sense

oligonucleotide (15 ug) had no significant effect on NPY-induced feeding. Two weeks after the antisense oligonucleotide treatment, feeding was once again elicited by the injection of NPY. Hypothalamic **CREB** protein was also reduced significantly two days after the **CREB antisense** oligonucleotide treatment. These results suggest that activation of **CREB**, probably through phosphorylation, may be a necessary event for the signal transduction of NPY stimulation into feeding behavior.

L10 ANSWER 4 OF 46 MEDLINE on STN
ACCESSION NUMBER: 2001221808 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11311197
TITLE: The role of cyclic AMP response element-binding protein in testosterone-induced differentiation of granular convoluted tubule cells in the rat submandibular gland.
AUTHOR: Kim J; Amano O; Wakayama T; Takahagi H; Iseki S
CORPORATE SOURCE: Department of Anatomy, School of Medicine, Kanazawa University, 13-1 Takaramachi, 920-8640, Kanazawa, Japan.
SOURCE: Archives of oral biology, **(2001 Jun)** 46 (6) 495-507.
Journal code: 0116711. ISSN: 0003-9969.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Dental Journals; Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010813
Last Updated on STN: 20010813
Entered Medline: 20010809

AB The postnatal development of granular convoluted tubules (GCT) in the duct system of the rodent submandibular gland is known to be androgen-dependent, but the underlying molecular mechanism is unclear. To test the possible role of the transcription factor, cyclic AMP response element-binding protein (**CREB**), in the androgen-induced differentiation of GCT, the effect of testosterone on the expression and localization of epidermal growth factor (EGF), a marker of GCT cells, and of **CREB** was examined in the submandibular glands of immature 3-week-old rats. Northern blotting demonstrated increases in both EGF and **CREB** mRNA 1-4 days after testosterone administration. Immunoprecipitation also indicated that **CREB** protein was increased in amount with testosterone administration, and that induced **CREB** was phosphorylated at the serine residue as in the active form of **CREB**. In situ hybridization demonstrated that cells with **CREB** mRNA signal first appeared in the distal portions of striated ducts at 1 day and had increased in number by 4 days after giving testosterone, when cells with EGF mRNA signal became evident in the same duct portions. Immunohistochemistry also showed the occurrence of **CREB** protein in the nuclei of duct epithelial cells before their differentiation into EGF-positive GCT cells. Finally, pieces of submandibular gland from immature rats were cultured in vitro and their expression of EGF mRNA analysed by the reverse transcriptase-polymerase chain reaction. Testosterone in the medium caused a marked enhancement of EGF expression in the gland in 1-4 days, which was attenuated by simultaneous administration of the **antisense** oligonucleotide for **CREB** as well as that for the androgen receptor. These results suggest the **CREB** is upregulated by androgen and has a crucial role in androgen-induced differentiation of GCT in the duct system of the rat submandibular gland.

L10 ANSWER 5 OF 46 MEDLINE on STN
ACCESSION NUMBER: 2001180864 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11236939

TITLE: **CREB antisense** oligonucleotides induce non-apoptotic cell death in proliferating leukemia cells, but not normal hematopoietic cells, by a bizarre non-**antisense** mechanism.

AUTHOR: Saeki K; Yuo A; Koizumi M; Fujiwara K; Kaneko M; Takaku F; Yazaki Y

CORPORATE SOURCE: Department of Hematology, Research Institute, International Medical Center of Japan, Tokyo.

SOURCE: Leukemia : official journal of the Leukemia Society of America, Leukemia Research Fund, U.K, **(2001 Feb)** 15 (2) 238-45.
Journal code: 8704895. ISSN: 0887-6924.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200103

ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010329

AB We report that **antisense** phosphorothioate oligodeoxyribonucleotides (PS-ODNs) against cyclic AMP response element-binding protein (**CREB**) induce the death of human leukemia cell lines including HL-60, Kasumi-1 and K562, OCI-AML1a and also primary leukemia cells isolated from patients with acute myelocytic leukemia and chronic myelocytic leukemia in blastic crisis. In contrast, normal human bone marrow CD34+ cells and normal peripheral blood lymphocytes were resistant to the antisense-mediated cell death. We found that antisense-treated HL-60 cells had prominent nuclear fragmentations but lacked apoptotic features including internucleosomal DNA cleavage and TUNEL positivity. Cell cycle analysis demonstrated a remarkable reduction in G1 phase population along with a mild accumulation of S phase and good preservation of G2/M phase, indicating cells died at G2/M without cycling into G1 phase. None of the sense-sequenced PS-ODNs induced cell death. Further, neither the expression nor the message of **CREB** protein was reduced by **antisense** treatment, indicating that cell death was mediated by a non-**antisense** mechanism. On the other hand, no consensus oligonucleotide sequence for cell death induction was detected. Rather, we found a good correlation between the melting temperatures and the anti-proliferative activities of the oligonucleotides. Thus, **CREB antisense** PS-ODNs selectively induce a non-apoptotic cell death in leukemic cells by an unknown hybridization-dependent mechanism.

L10 ANSWER 6 OF 46 MEDLINE on STN

ACCESSION NUMBER: 2000384924 MEDLINE

DOCUMENT NUMBER: PubMed ID: 10841885

TITLE: **CREB** contributes to the increased neurite outgrowth of sensory neurons induced by vasoactive intestinal polypeptide and activity-dependent neurotrophic factor.

AUTHOR: White D M; Walker S; Brenneman D E; Gozes I

CORPORATE SOURCE: Department of Anaesthesia and Pain Management, Royal North Shore Hospital, University of Sydney, N.S.W., 2065, St Leonards, Australia.. dmwhite@med.usyd.edu.au

SOURCE: Brain research, **(2000 Jun 16)** 868 (1) 31-8.
Journal code: 0045503. ISSN: 0006-8993.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200008

ENTRY DATE: Entered STN: 20000818

Last Updated on STN: 20000818
Entered Medline: 20000804

AB Our recent experiments suggest that vasoactive intestinal polypeptide (VIP) enhances neurite outgrowth of dissociated rat dorsal root ganglion cells, indirectly, via the release of a trophic factor from the spinal cord. In this study, we have examined the possible contribution of activity-dependent neurotrophic factor (ADNF) to the trophic actions of VIP. In addition, as we have shown that the factor mediating the trophic actions of VIP acts via protein kinase A we have also examined the contribution of **CREB**, which is a transcription factor activated by protein kinase A. As previously shown, supernatant taken from spinal cord incubated with VIP, significantly increased the percentage of sensory neurons with neurites. Antiserum against ADNF attenuated the trophic effect of the VIP-conditioned supernatant. Consistently, the ADNF agonist, ADNF(14) (0.001-0.1 fM), significantly enhanced the percentage of cells with neurite outgrowth. Furthermore, the trophic action of ADNF(14) was attenuated by a protein kinase A inhibitor, Rp-cAMPS, whereas the inactive isomer, Sp-cAMPS, had no effect. Preincubation of cells with 5 mcM **CREB antisense** oligonucleotides, attenuated the increase in neurite outgrowth induced by either the supernatant or ADNF(14). The sense oligonucleotide had no influence on the enhanced neurite outgrowth. We also found that both the supernatant and ADNF(14) induced an increase in the percentage of cells expressing phosphorylated **CREB**. The data suggests that VIP induces a release of neurotrophic factors, such as ADNF, which enhance neurite outgrowth. In addition, protein kinase A and **CREB** appear to contribute to the neurotrophic actions of VIP and ADNF. The mechanisms underlying the neurotrophic action of VIP, may have important implications for sprouting and/or synaptic reorganization of central terminals of sensory neurons, which may contribute to neuropathic pain that commonly occurs following peripheral nerve damage.

L10 ANSWER 7 OF 46 MEDLINE on STN
ACCESSION NUMBER: 1999337781 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10407170
TITLE: **CREB** mediates the cAMP-responsiveness of the tyrosine hydroxylase gene: use of an **antisense** RNA strategy to produce **CREB**-deficient PC12 cell lines.
AUTHOR: Piech-Dumas K M; Tank A W
CORPORATE SOURCE: Department of Pharmacology and Physiology, University of Rochester Medical Center, Box 711, 601 Elmwood Ave., Rochester, NY 14642, USA.. piechk@pharmacol.rochester.edu
CONTRACT NUMBER: AG00107 (NIA)
DA 05014 (NIDA)
DA0723 (NIDA)
SOURCE: Brain research. Molecular brain research, **(1999 Jul 5)** 70 (2) 219-30.
Journal code: 8908640. ISSN: 0169-328X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19990921
Last Updated on STN: 19990921
Entered Medline: 19990908

AB cAMP initiates the PKA signaling cascade in rat pheochromocytoma PC12 cells, resulting in transcriptional activation of the tyrosine hydroxylase (TH) gene. This effect is mediated primarily through the cAMP responsive element (CRE), located at position -45 to -38 within the TH gene promoter. In this study, we applied an **antisense** RNA strategy to evaluate the role of the cAMP responsive element binding protein (**CREB**)

in regulating TH gene expression. **CREB antisense** RNA expression vectors were stably introduced into PC12 cells to generate cell lines deficient in **CREB**. **CREB** protein and mRNA levels were diminished up to 90% in the stably transfected cell lines. Promoter analysis experiments demonstrated that cAMP-mediated inducibility of either TH gene proximal promoter activity or the activity of the TH CRE by itself fused upstream of a basal promoter was diminished in **CREB** -deficient cell lines. PKA activity in the **CREB**-deficient cell lines was comparable to the activity in control cell lines. In addition, neither ATF1, nor CREM proteins were significantly down-regulated in the **CREB**-deficient cells. Most significantly, the cAMP-inducibility of endogenous TH mRNA was completely blocked in the **CREB** -deficient cells, indicating that the response of the endogenous gene to cAMP was dependent on **CREB**. These results support the hypothesis that **CREB** (not other CRE-binding proteins) is the key transcription factor that is required for regulating TH gene expression in response to cAMP. Furthermore, our studies indicate that these **CREB**-deficient PC12 cells are excellent tools to study the participation of **CREB** in gene regulation.

L10 ANSWER 8 OF 46 MEDLINE on STN
ACCESSION NUMBER: 1999017410 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9802424
TITLE: NPY upregulates genes containing cyclic AMP response element in human neuroblastoma cell lines bearing Y1 and Y2 receptors: involvement of **CREB**.
AUTHOR: Sheriff S; Dayal R; Kasckow J; Regmi A; Chance W; Fischer J; Balasubramaniam A
CORPORATE SOURCE: Department of Surgery, University of Cincinnati, College of Medicine, OH 45267, USA.. sherifs@ucbeh.san.uc.edu
CONTRACT NUMBER: GM 47122 (NIGMS)
SOURCE: Regulatory peptides, **(1998 Sep 25)** 75-76 309-18. Journal code: 8100479. ISSN: 0167-0115.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 19990202
Last Updated on STN: 19990202
Entered Medline: 19990119

AB Four NPY receptor subtypes have been cloned, and shown to be coupled to both Ca2+ and cAMP. However, very little is known about the downstream elements mediating NPY actions. It has recently been demonstrated in our laboratory that intrahypothalamic (i.h.t.) administration of NPY induces hypothalamic CaM kinase activity, cyclic AMP response element binding protein (**CREB**) phosphorylation and cyclic AMP response element (CRE) binding activity in rat hypothalamic nuclear proteins. In the present study, we have investigated whether these changes in CRE binding transcriptional factors activated by NPY results in gene regulation using a human neuroblastoma cell line (SK-N-BE2). This cell line which expresses the Y2 subtype of NPY receptors was transfected with a fusion gene containing 1.305 kb of human CRF 5' flanking region with a perfect palindromic CRE site linked to firefly luciferase gene. NPY treatment increased CaM kinase II activity, **CREB** phosphorylation and CRE binding in these cells. In transfected cells, luciferase activity was also increased by NPY (1.8-4-fold) within 4 h of treatment. Moreover, forskolin (7-30-fold), which stimulates cAMP production, and thapsigargin (6-8-fold), which mobilizes intracellular calcium, also increased luciferase activity within 4 h of treatment. PMA (phorbol-12-myristate-13-acetate), an activator of protein kinase-C, induced luciferase activity by 1.8-fold. NPY augmented forskolin-stimulated luciferase activity from 11-

to 15-fold, but had no significant effect on thapsigargin-induced luciferase activity. These findings suggest that activation of protein kinase A (PKA) or CaM kinase leads to the induction of fusion gene. NPY treatment upregulated fusion gene expression through Ca2+ pathway in SK-N-BE2 cell line. Pretreatment with **CREB antisense**, but not the sense oligodeoxynucleotides, inhibited forskolin-, thapsigargin- and NPY-stimulated luciferase activity. However, **CREB** sense or **antisense** oligodeoxynucleotide treatment had no effect on PMA-stimulated luciferase activity. Furthermore, NPY induced CRE binding activity and the expression of CRE containing Y1 receptor gene in SK-N-MC cell line. These findings suggest that NPY can upregulate CRE containing reporter gene including Y1 receptor gene and NPY-induced reporter gene regulation in SK-N-BE2 cells is mediated by intracellular Ca2+ and **CREB** protein.

L10 ANSWER 9 OF 46 MEDLINE on STN
ACCESSION NUMBER: 97477460 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9334416
TITLE: cAMP response element-binding protein in the amygdala is required for long- but not short-term conditioned taste aversion memory.
AUTHOR: Lamprecht R; Hazvi S; Dudai Y
CORPORATE SOURCE: Department of Neurobiology, The Weizmann Institute of Science, Rehovot 76100, Israel.
SOURCE: Journal of neuroscience : official journal of the Society for Neuroscience, **(1997 Nov 1)** 17 (21) 8443-50. Journal code: 8102140. ISSN: 0270-6474.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 20000303
Entered Medline: 19971120

AB In conditioned taste aversion (CTA) organisms learn to avoid a taste if the first encounter with that taste is followed by transient poisoning. The neural mechanisms that subserve this robust and long-lasting association of taste and malaise have not yet been elucidated, but several brain areas have been implicated in the process, including the amygdala. In this study we investigated the role of amygdala in general, and the cAMP response element-binding protein (**CREB**) in the amygdala in particular, in CTA learning and memory. Toward that end, we combined antisense technology in vivo with behavioral, molecular, and histochemical analysis. Local microinjection of phosphorothioate-modified oligodeoxynucleotides (ODNs) **antisense** to **CREB** into the rat amygdala several hours before CTA training transiently reduced the level of **CREB** protein during training and impaired CTA memory when tested 3-5 d later. In comparison, sense ODNs had no effect on memory. The effect of antisense was not attributable to differential tissue damage and was site-specific. **CREB antisense** in the amygdala had no effect on retrieval of CTA memory once it had been formed, and did not affect short-term CTA memory. We propose that the amygdala, specifically the central nucleus, is required for the establishment of long-term CTA memory in the behaving rat; that the process involves long-term changes, subserved by CRE-regulated gene expression, in amygdala neurons; and that the amygdala may retain some CTA-relevant information over time rather than merely modulating the gustatory trace during acquisition of CTA.

L10 ANSWER 10 OF 46 MEDLINE on STN
ACCESSION NUMBER: 97461633 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9315909

TITLE: **CREB** (cAMP response element-binding protein) in the locus coeruleus: biochemical, physiological, and behavioral evidence for a role in opiate dependence.
AUTHOR: Lane-Ladd S B; Pineda J; Boundy V A; Pfeuffer T; Krupinski J; Aghajanian G K; Nestler E J
CORPORATE SOURCE: Department of Psychiatry, Yale University School of Medicine and Connecticut Mental Health Center, New Haven, Connecticut 06508, USA.
CONTRACT NUMBER: DA00203 (NIDA)
DA08227 (NIDA)
SOURCE: Journal of neuroscience : official journal of the Society for Neuroscience, **(1997 Oct 15)** 17 (20) 7890-901.
Journal code: 8102140. ISSN: 0270-6474.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 19971105
Last Updated on STN: 20000303
Entered Medline: 19971023

AB Chronic morphine administration increases levels of adenylyl cyclase and cAMP-dependent protein kinase (PKA) activity in the locus coeruleus (LC), which contributes to the severalfold activation of LC neurons that occurs during opiate withdrawal. A role for the transcription factor cAMP response element-binding protein (**CREB**) in mediating the opiate-induced upregulation of the cAMP pathway has been suggested, but direct evidence is lacking. In the present study, we first demonstrated that the morphine-induced increases in adenylyl cyclase and PKA activity in the LC are associated with selective increases in levels of immunoreactivity of types I and VIII adenylyl cyclase and of the catalytic and type II regulatory subunits of PKA. We next used **antisense** oligonucleotides directed against **CREB** to study the role of this transcription factor in mediating these effects. Infusion (5 d) of **CREB antisense** oligonucleotide directly into the LC significantly reduced levels of **CREB** immunoreactivity. This effect was sequence-specific and not associated with detectable toxicity. **CREB antisense** oligonucleotide infusions completely blocked the morphine-induced upregulation of type VIII adenylyl cyclase but not of PKA. The infusions also blocked the morphine-induced upregulation of tyrosine hydroxylase but not of Gialpha, two other proteins induced in the LC by chronic morphine treatment. Electrophysiological studies revealed that intra-LC antisense oligonucleotide infusions completely prevented the morphine-induced increase in spontaneous firing rates of LC neurons in brain slices. This blockade was completely reversed by addition of 8-bromo-cAMP (which activates PKA) but not by addition of forskolin (which activates adenylyl cyclase). Intra-LC infusions of **CREB antisense** oligonucleotide also reduced the development of physical dependence to opiates, based on attenuation of opiate withdrawal. Together, these findings provide the first direct evidence that **CREB** mediates the morphine-induced upregulation of specific components of the cAMP pathway in the LC that contribute to physical opiate dependence.

L10 ANSWER 11 OF 46 MEDLINE on STN
ACCESSION NUMBER: 97226016 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9122258
TITLE: Antisense oligodeoxynucleotide-mediated disruption of hippocampal cAMP response element binding protein levels impairs consolidation of memory for water maze training.
AUTHOR: Guzowski J F; McGaugh J L
CORPORATE SOURCE: Center for the Neurobiology of Learning and Memory, University of California, Irvine 92697-3800, USA..

jguzowsk@darwin.bio.uci.edu
CONTRACT NUMBER: MH12526 (NIMH)
T32A600096
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, **(1997 Mar 18)** 94 (6) 2693-8.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-X14788
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970506
Last Updated on STN: 19970506
Entered Medline: 19970424

AB Extensive evidence suggests that long term memory (LTM) formation is dependent on the activation of neuronal second messenger systems and requires protein synthesis. The cAMP response element binding protein (**CREB**) is a constitutively expressed regulatory transcription factor that couples changes in second messenger levels to changes in cellular transcription. Several recent studies suggest that **CREB** and related transcription factors regulate gene expression necessary for neuronal plasticity and LTM. However, the role of **CREB**, within defined mammalian brain structures, in mediating the cellular events underlying LTM formation has not been investigated. We examined whether **CREB**-mediated transcription within the dorsal hippocampus is critical to LTM consolidation of water maze spatial training, which is known to depend on dorsal hippocampal function. Pretraining infusions of **antisense** oligodeoxynucleotides (ODN) directed against **CREB** mRNA were used to disrupt hippocampal **CREB** protein levels in adult rats. Control groups received pretraining infusions of ODN of the same base composition but in a randomized order (scrambled ODN) or buffer. Task acquisition and memory up to 4 h (i.e., short term memory) were similar in **CREB antisense** ODN and control groups. In contrast, **CREB antisense** ODN-infused rats exhibited significantly impaired memory 48 h later (i.e., LTM). Moreover, administration of antisense ODN 1 day after training did not affect subsequent retention performance. These findings provide the first evidence that **CREB**-mediated transcription is integral to hippocampal-dependent memory consolidation processes.

L10 ANSWER 12 OF 46 MEDLINE on STN
ACCESSION NUMBER: 97190347 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9038229
TITLE: Tyrosine hydroxylase gene promoter activity is regulated by both cyclic AMP-responsive element and AP1 sites following calcium influx. Evidence for cyclic amp-responsive element binding protein-independent regulation.
AUTHOR: Nagamoto-Combs K; Piech K M; Best J A; Sun B; Tank A W
CORPORATE SOURCE: Department of Pharmacology and Physiology, and the Neuroscience Program, University of Rochester Medical Center, Rochester, New York 14642, USA.
CONTRACT NUMBER: DA07232 (NIDA)
SOURCE: Journal of biological chemistry, **(1997 Feb 28)** 272 (9) 6051-8.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970424

Last Updated on STN: 20021218
Entered Medline: 19970415

AB Membrane depolarization of PC12 cells using 50 mM KCl leads to induction of tyrosine hydroxylase (TH) mRNA. This induction of TH mRNA is apparently due to increased TH gene promoter activity mediated by the influx of Ca2+. In PC12 cells transiently transfected with a chimeric gene expressing chloramphenicol acetyltransferase (CAT) driven by the proximal TH gene 5'-flanking region, 50 mM KCl increases TH gene promoter activity 3-4-fold. Promoter analysis utilizing TH-CAT constructs containing mutagenized sequences indicates that this response to the depolarization-mediated influx of Ca2+ is primarily dependent on both the TH cAMP-responsive element (CRE) and TH activating protein-1 (AP1) site. Minimal promoter constructs that contain a single copy of either the TH CRE or TH AP1 site fused upstream of the TH gene basal promoter are only modestly responsive or nonresponsive, respectively, to depolarization. However, both these constructs are strongly responsive to the calcium ionophore, A23187. Gel shift assays indicate that TH AP1 complex formation is dramatically increased after treatment with either 50 mM KCl or A23187. Using antibodies to transcription factors of the Fos and Jun families, we show that the nuclear proteins comprising the inducible TH AP1 complex include c-Fos, c-Jun, JunB, and JunD. In cAMP-responsive element binding protein (**CREB**)-deficient cell lines that express **antisense** RNA complementary to **CREB** mRNA, the response of the TH gene promoter to cyclic AMP is dramatically inhibited, but the response to A23187 remains robust. This result indicates that transcription factors other than **CREB** can participate in the Ca2+-mediated regulation of the TH gene. In summary, our results support the hypothesis that regulation of the TH gene by Ca2+ is mediated by mechanisms involving both the TH CRE and TH AP1 sites and that transcription factors other than or in addition to **CREB** participate in this response.

L10 ANSWER 13 OF 46 MEDLINE on STN
ACCESSION NUMBER: 97188494 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9037079
TITLE: Morphological plasticity of dendritic spines in central neurons is mediated by activation of cAMP response element binding protein.
AUTHOR: Murphy D D; Segal M
CORPORATE SOURCE: Laboratory of Neurobiology, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD 20892, USA.. diane@codon.nih.gov
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, **(1997 Feb 18)** 94 (4) 1482-7.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970407
Last Updated on STN: 19970407
Entered Medline: 19970327

AB While evidence has accumulated in favor of cAMP-associated genomic involvement in long-term synaptic plasticity, the mechanisms downstream of the activated nucleus that underlie these changes in neuronal function remain mostly unknown. Dendritic spines, the locus of excitatory interaction among central neurons, are prime candidates for long-term synaptic modifications. We now present evidence that links phosphorylation of the cAMP response element binding protein (**CREB**) to formation of new spines; exposure to estradiol doubles the density of dendritic spines in cultured hippocampal neurons, and concomitantly causes

a large increase in phosphorylated **CREB** and in **CREB** binding protein. Blockade of cAMP-regulated protein kinase A eliminates estradiol-evoked spine formation, as well as the **CREB** and **CREB** binding protein responses. A specific **antisense** oligonucleotide eliminates the phosphorylated **CREB** response to estradiol as well as the formation of new dendritic spines. These results indicate that **CREB** phosphorylation is a necessary step in the process leading to generation of new dendritic spines.

L10 ANSWER 14 OF 46 MEDLINE on STN
ACCESSION NUMBER: 97047190 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8892110
TITLE: Treatment of oligodendrocytes with **antisense** deoxyoligonucleotide directed against **CREB** mRNA: effect on the cyclic AMP-dependent induction of myelin basic protein expression.
AUTHOR: Sato-Bigbee C; DeVries G H
CORPORATE SOURCE: Department of Biochemistry and Molecular Biophysics, Medical College of Virginia, Virginia Commonwealth University, Richmond 23298-0614, USA.
SOURCE: Journal of neuroscience research, **(1996 Oct 1)** 46 (1) 98-107.
Journal code: 7600111. ISSN: 0360-4012.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970523
Last Updated on STN: 20021015
Entered Medline: 19970513

AB We have shown previously that in oligodendrocytes, the transcription factor cyclic AMP response element binding protein (**CREB**) is maximally expressed immediately prior to the most rapid period of myelination in rat brain. We have begun to investigate the role of this protein during myelination by downregulating **CREB** synthesis in cultured oligodendrocytes using an **antisense** deoxyoligonucleotide directed against **CREB** mRNA. Neonatal oligodendrocytes were grown for 4 days in a chemically defined medium (CDM) after which intracellular delivery of **CREB** **antisense** oligonucleotide was facilitated by using a liposome preparation. Control cultures were treated in a similar manner but in the presence of **CREB** sense oligomer. Immediately after transfection, cells were cultured for 3 days in CDM in the presence or absence of the cyclic AMP (cAMP) analogue N6, O21-dibutyryl cAMP (db-cAMP). In these cultures, myelin basic protein (MBP) expression was investigated by immunocytochemistry and Western blot analysis. Treatment of control cultures with db-cAMP resulted in a significant increase in the number of MBP positive cells which was abolished when the cells were treated with **CREB** **antisense** oligonucleotide. MBP positive cells in control cultures treated with db-cAMP have extended and highly branched MBP positive processes. In contrast, MBP positive cells in either control cultures grown in the absence of db-cAMP or cultures grown in the presence of db-cAMP but treated with **CREB** **antisense** oligonucleotide showed shorter and less complex processes and the MBP immunoreactivity appeared to be concentrated in the cell body. These observations suggest that **CREB** is at least one of the mediators in the induction of oligodendrocyte differentiation by cAMP.

L10 ANSWER 15 OF 46 MEDLINE on STN
ACCESSION NUMBER: 96217278 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8641191

TITLE: Major role of 3',5'-cyclic adenosine monophosphate-dependent protein kinase A pathway in corticotropin-releasing factor gene expression in the rat hypothalamus in vivo.
AUTHOR: Itoi K; Horiba N; Tozawa F; Sakai Y; Sakai K; Abe K; Demura H; Suda T
CORPORATE SOURCE: Third Department of Medicine, Hirosaki University School of Medicine, Japan.
SOURCE: Endocrinology, **(1996 Jun)** 137 (6) 2389-96.
Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199607
ENTRY DATE: Entered STN: 19960726
Last Updated on STN: 19960726
Entered Medline: 19960718

AB To assess whether the cAMP-dependent protein kinase-A and/or the diacylglycerol-dependent protein kinase C (PKC) pathways play important roles in the activation of CRF neurons in vivo under physiological conditions, we tested the effect of microinjection of 8-bromo-cAMP (8-Br-cAMP) or 12-O-tetradecanoyl phorbol 13-acetate (TPA) into both paraventricular nuclei (PVN) of the hypothalamus in conscious rats. Both 8-Br-cAMP and TPA increased plasma ACTH concentrations and the POMC messenger RNA (mRNA) concentrations in the anterior pituitary. While injection of 8-Br-cAMP also increased CRF mRNA concentrations in hypothalamic tissue containing the PVN, TPA injection had no effect on CRF mRNA concentrations there. During insulin-induced hypoglycemia, which stimulates CRF gene expression and release, c-fos and c-jun mRNA increases in the hypothalamic tissue preceded the increase in the CRF mRNA level after insulin-induced hypoglycemia. **Antisense** oligodeoxyribonucleotides (oligos) directed against c-fos, c-jun, or the cAMP response element binding protein (**CREB**) mRNA were injected into both PVN before insulin-induced hypoglycemia to assess whether activator protein-1 or **CREB** mediates transcriptional activation of CRF during hypoglycemia. Only **antisense** oligo against **CREB** mRNA reduced the CRF mRNA level after insulin-induced hypoglycemia. These results suggest that protein kinase A may transduce intracellular signals in CRF neurons under physiological conditions and raises the possibility that **CREB** may be involved in stress-induced CRF gene expression.

L10 ANSWER 16 OF 46 MEDLINE on STN
ACCESSION NUMBER: 96135082 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8558448
TITLE: Regulation of **CREB** expression: in vivo evidence for a functional role in morphine action in the nucleus accumbens.
AUTHOR: Widnell K L; Self D W; Lane S B; Russell D S; Vaidya V A; Miserendino M J; Rubin C S; Duman R S; Nestler E J
CORPORATE SOURCE: Department of Psychiatry, Yale University School of Medicine, New Haven, Connecticut, USA.
CONTRACT NUMBER: DA00203 (NIDA)
DA07359 (NIDA)
DA08227 (NIDA)
+
SOURCE: Journal of pharmacology and experimental therapeutics, **(1996 Jan)** 276 (1) 306-15.
Journal code: 0376362. ISSN: 0022-3565.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199602
ENTRY DATE: Entered STN: 19960312
Last Updated on STN: 20000303
Entered Medline: 19960226

AB Previous work has shown that chronic opiate administration regulates protein components of the cAMP signaling pathway, specifically in the nucleus accumbens (NAc), a brain region implicated in the reinforcing properties of opiates, and that such adaptations may contribute to changes in reinforcement mechanisms that characterize opiate addiction. In the present study, we examined a possible role for the transcription factor cAMP response element-binding protein (**CREB**) in mediating these long-term effects of opiates in the NAc. Chronic, but not acute, morphine administration was found to decrease levels of **CREB** immunoreactivity in the NAc, an effect not seen in other brain regions studied. The functional significance of this **CREB** down-regulation was then investigated by the use of an **antisense** oligonucleotide strategy that produces a specific and sustained decrease in **CREB** levels in the NAc, without detectable toxicity. It was found that the **antisense** oligonucleotide-induced reduction in **CREB** levels mimicked the effect of morphine on certain, but not all, cAMP pathway proteins in this brain region, whereas a large number of other signal transduction proteins tested were unaffected by this treatment. Our results support a role for **CREB** in autoregulation of the cAMP pathway in the nervous system, as well as in mediating some of the effects of morphine on this signaling pathway in the NAc.

L10 ANSWER 17 OF 46 MEDLINE on STN
ACCESSION NUMBER: 96065242 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7583020
TITLE: Dopamine regulation of transcription factor-target interactions in rat striatum.
AUTHOR: Hyman S E; Cole R L; Konradi C; Kosofsky B E
CORPORATE SOURCE: Laboratory of Molecular and Developmental Neuroscience, Massachusetts General Hospital, Charlestown 02129, USA.
SOURCE: Chemical senses, **(1995 Apr)** 20 (2) 257-60. Ref: 24
Journal code: 8217190. ISSN: 0379-864X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199511
ENTRY DATE: Entered STN: 19960124
Last Updated on STN: 19960124
Entered Medline: 19951130

AB Transcriptional regulation is an important mechanism by which neurons adapt to environmental stimuli. The indirect dopamine agonists, amphetamine and cocaine have been shown to induce expression of immediate early genes, such as c-fos, and neuropeptide genes, such as prodynorphin in the rat striatum. Here we show that phosphorylation of transcription factor **CREB** is a critical early event coupling dopamine stimulation to gene regulation. **CREB** interacts with functional regulatory elements in both the c-fos and prodynorphin genes, and is phosphorylated in response to dopamine in a D1 dopamine receptor-dependent manner. In addition, we show by intra-striatal injection of **antisense** oligonucleotides directed against **CREB** mRNA, that **CREB** protein is required for c-fos induction by amphetamine.

L10 ANSWER 18 OF 46 MEDLINE on STN
ACCESSION NUMBER: 94365703 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8083758
TITLE: Amphetamine regulates gene expression in rat striatum via transcription factor **CREB**.
AUTHOR: Konradi C; Cole R L; Heckers S; Hyman S E
CORPORATE SOURCE: Laboratory of Molecular and Developmental Neuroscience, Massachusetts General Hospital, Charlestown 02129.
CONTRACT NUMBER: DA07134 (NIDA)
DA07282 (NIDA)
MH44160 (NIMH)
SOURCE: Journal of neuroscience : official journal of the Society for Neuroscience, **(1994 Sep)** 14 (9) 5623-34.
Journal code: 8102140. ISSN: 0270-6474.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199410
ENTRY DATE: Entered STN: 19941021
Last Updated on STN: 20021015
Entered Medline: 19941012

AB Amphetamine is a psychostimulant drug of abuse that can produce long-lived changes in behavior including sensitization and dependence. The neural substrates of these drug effects remain unknown, but based on their prolonged time course, we hypothesize that they involve drug-induced alterations in gene expression. It has recently been demonstrated that amphetamine regulates the expression of several genes, including c-fos, via dopamine D1 receptors in rat striatum. Here we report that amphetamine induces phosphorylation of transcription factor cAMP response element binding protein (**CREB**) in rat striatum in vivo and that dopamine D1 receptor stimulation induces phosphorylation of **CREB** within specific complexes bound to cAMP regulatory elements. In addition, we show by **antisense** injection that **CREB** is necessary for c-fos induction by amphetamine in vivo. Since **CREB** has been implicated in the activation of a number of immediate-early genes as well as several neuropeptide genes, **CREB** phosphorylation may be an important early nuclear event mediating long-term consequences of amphetamine administration.

L10 ANSWER 19 OF 46 MEDLINE on STN
ACCESSION NUMBER: 93376488 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8396235
TITLE: Member of the **CREB**/ATF protein family, but not **CREB** alpha plays an active role in BLV tax trans activation in vivo.
AUTHOR: Kiss-Toth E; Paca-uccaralertkun S; Unk I; Boros I
CORPORATE SOURCE: Institute of Biochemistry, Hungarian Academy of Sciences, Szeged.
SOURCE: Nucleic acids research, **(1993 Aug 11)** 21 (16) 3677-82.
Journal code: 0411011. ISSN: 0305-1048.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199310
ENTRY DATE: Entered STN: 19931022
Last Updated on STN: 19970203
Entered Medline: 19931001

AB The trans activator protein of Bovine Leukaemia Virus (tax) increases the rate of transcription from the virus promoter through 21 bp sequences located in three tandem copies in the virus LTR. Based on data obtained

by three different experimental approaches we concluded that the central CRE-like motif found in each of the BLV 21 bp repeats plays an important and indispensable role in tax mediated trans activation. These include (i) in vivo analysis of the function of mutant 21 bp sequences in transient transfection, (ii) gel mobility shift assay to show that **CREB** binds to BLV 21 bp repeats in vitro and (iii) the demonstration that the production of **antisense CREB** mRNA inhibits tax trans activation. Further studies with different deletion mutant **CREB** proteins suggest that although **CREB** alpha can interact with factors involved in BLV trans activation, it does not promote transcription initiation; consequently some other member/s of the **CREB**/ATF family must be involved.

L10 ANSWER 20 OF 46 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:329962 BIOSIS
DOCUMENT NUMBER: PREV200200329962
TITLE: **Antisense** cAMP-responsive element binding protein (**CREB**) cDNA transfer blocks the stimulatory effect of high glucose and activating transcription factor-2 (ATF-2) on angiotensinogen (ANG) gene expression and induction of hypertrophy in rat renal proximal tubular cells.
AUTHOR(S): Zhang, Shao-Ling [Reprint author]; Chen, Xing [Reprint author]; Filep, Janos G.; Tang, Shiow-Shih; Ingelfinger, Julie R.; Chan, John S. D. [Reprint author]
CORPORATE SOURCE: Res. Center, Centre Hospitalier de l'Univ. de Montreal-Hotel-Dieu, Montreal, PQ, Canada
SOURCE: Journal of the American Society of Nephrology, (**September, 2001**) Vol. 12, No. Program and Abstract Issue, pp. 605A. print.
Meeting Info.: ASN (American Society of Nephrology)/ISN (International Society of Nephrology) World Congress of Nephrology. San Francisco, CA, USA. October 10-17, 2001.
CODEN: JASNEU. ISSN: 1046-6673.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Jun 2002
Last Updated on STN: 12 Jun 2002

L10 ANSWER 21 OF 46 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:547091 BIOSIS
DOCUMENT NUMBER: PREV200100547091
TITLE: Characterization of the mouse adenylyl cyclase type VIII gene promoter.
AUTHOR(S): Chao, J. R. [Reprint author]; Ni, Y. G.; DiLeone, R. J. [Reprint author]; Chen, J. S.; Rahman, Z. [Reprint author]; Nestler, E. J. [Reprint author]
CORPORATE SOURCE: Dept. of Psychiatry, UT Southwestern Med Ctr, Dallas, TX, USA
SOURCE: Society for Neuroscience Abstracts, (**2001**) Vol. 27, No. 1, pp. 1215. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience. San Diego, California, USA. November 10-15, 2001.
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Nov 2001

Last Updated on STN: 25 Feb 2002

AB Chronic morphine administration upregulates several components of the cAMP pathway in the locus coeruleus, including adenylyl cyclase (AC) types 1 and 8, protein kinase A, and the transcription factor **CREB**. Similar effects are seen in several other brain regions. Upregulation of AC8 may be mediated by **CREB**, since infusion of **antisense** oligonucleotides to **CREB** into the locus coeruleus blocks the morphine-induced increase in AC8 expression. This is supported by in vitro studies demonstrating that a 4.5 kb fragment of the AC8 promoter containing a cAMP response element (CRE) is activated by forskolin (which stimulates the cAMP pathway) in cell lines and primary cultures of rat striatal neurons. AC8 promoter deletion and point mutations, gel shift assays, and co-transfection studies demonstrate that AC8 promoter activation by forskolin is specifically mediated by **CREB** family members at the canonical CRE site. Transgenic mice containing a 90 kb BAC, including 35 kb of the AC8 promoter driving expression of the reporter gene EGFP, are being constructed to assess the in vivo regulation of the AC8 promoter. Moreover, the specific effect of CRE regulation of AC8 promoter activity in vivo will be studied in reporter mice containing the identical 90 kb reporter construct described above with the exception of a substitution mutation at the consensus CRE site in the AC8 promoter. Together, these in vitro and reporter mice studies will further the understanding of AC8 gene regulation by **CREB** and contribute to the study of **CREB**-dependent neural plasticity in drug addiction.

L10 ANSWER 22 OF 46 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:480589 BIOSIS
DOCUMENT NUMBER: PREV200100480589
TITLE: **CREB antisense** oligonucleotides induce death of human leukemic cells but not of normal hematopoietic cells by a bizarre non-**antisense** mechanism.
AUTHOR(S): Saeki, Kumiko; Kaneko, Masakatsu; Koizumi, Makoto; Fujiwara, Kosaku; Yuo, Akira
SOURCE: Experimental Hematology (Charlottesville), (**August, 2001**) Vol. 29, No. 8 Supplement 1, pp. 69. print.
Meeting Info.: 30th Annual Meeting of the International Society for Experimental Hematology. Tokyo, Japan. August 25-28, 2001.
CODEN: EXHMA6. ISSN: 0301-472X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Oct 2001
Last Updated on STN: 23 Feb 2002

L10 ANSWER 23 OF 46 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:346812 BIOSIS
DOCUMENT NUMBER: PREV200100346812
TITLE: Antisense oligodeoxyribonucleotide targeting cAMP response element-binding protein inhibits growth of rat submandibular gland In vitro.
AUTHOR(S): Amano, Osamu [Reprint author]; Iseki, Shoichi
CORPORATE SOURCE: Department of Anatomy, School of Medicine, Kanazawa University, 13-1 Takara-machi, Kanazawa, Ishikawa, 920-8640, Japan
SOURCE: Acta Histochemica et Cytochemica, (**2001**) Vol. 34, No. 2, pp. 111-117. print.
CODEN: ACHCBO. ISSN: 0044-5991.
DOCUMENT TYPE: Article
LANGUAGE: English

ENTRY DATE: Entered STN: 25 Jul 2001
Last Updated on STN: 19 Feb 2002

AB The transcription factor, cyclic AMP response element-binding protein (**CREB**), occurs in the nuclei of acinar cells of the rat submandibular gland during the early postnatal periods. To elucidate the role of **CREB** in the growth of submandibular gland, the effect of an **antisense** oligodeoxyribonucleotide (ODN) targeting **CREB** was examined in the organ culture system of neonatal rat submandibular gland. In the presence of **antisense-CREB** ODN in the culture media for 48 hr, a significant decrease in the growth of cultured gland was observed in terms of both the area of acinar epithelial tissue and 3H-thymidine-labeling index of acinar cells, with concomitant decrease in the nuclear immunoreactivity of **CREB** without any degenerative changes in the histology of the gland. In contrast, sense-**CREB** ODN exhibited no effect on acinar growth. Administration of the beta-adrenergic agonist isoproterenol (IPR) induced enhanced proliferation of acinar cells, which was also inhibited by **antisense-CREB** ODN. In contrast, the proliferation of connective tissue cells was neither enhanced by IPR nor inhibited by **antisense-CREB** ODN. These results suggest that the transcription factor **CREB** plays specific roles in the proliferation of submandibular gland acinar cells during the early postnatal periods.

L10 ANSWER 24 OF 46 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:114344 BIOSIS
DOCUMENT NUMBER: PREV200100114344
TITLE: Characterization of the mouse adenylyl cyclase type VIII gene promoter: activation by cAMP.
AUTHOR(S): Chao, J. R. [Reprint author]; Ni, Y. G.; Chen, J. S.; Rahman, Z.; Nestler, E. J.
CORPORATE SOURCE: Yale University School of Medicine, New Haven, CT, USA
SOURCE: Society for Neuroscience Abstracts, (**2000**) Vol. 26, No. 1-2, pp. Abstract No.-49.12. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 04-09, 2000. Society for Neuroscience.
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Mar 2001
Last Updated on STN: 15 Feb 2002

AB Chronic morphine administration upregulates several components of the cAMP pathway in the locus coeruleus, including types 1 and 8 adenylyl cyclase (AC), protein kinase A, and the transcription factor **CREB** (cAMP response element binding protein). Upregulation of AC8 may be mediated by **CREB**, since infusion of **antisense** oligonucleotides to **CREB** into the locus coeruleus blocks the morphine-induced increase in AC8 expression (Lane-Ladd et al. 1997). To study directly whether the AC8 gene is a target for **CREB**, we cloned a 4.5 kb fragment of the AC8 promoter from a mouse bacterial artificial chromosome. Nucleotide sequencing revealed consensus elements for several transcription factors, including a cAMP response element (CRE) within the presumed transcription initiation region as reported previously (Muglia et al. 1999). The 4.5 kb promoter fragment was subcloned into a luciferase reporter vector, and AC8 promoter activity was studied in SHSY5Y cells and in primary cultures of rat striatal neurons. Activation of the cAMP pathway by forskolin treatment increased luciferase activity in both cell types in a time-dependent manner. A series of deletion and point mutants demonstrated that the activation of the promoter by forskolin is mediated specifically via the canonical CRE site. In addition, cell extracts from

SHSY5Y cells and rat primary striatal neurons retarded an AC8 CRE oligonucleotide in gel mobility shift assays, and antibodies to **CREB** or ATF1 supershifted the bands. Finally, cotransfection of AC8-luciferase with a constitutively active form of **CREB**, **CREB**-VP16, dramatically enhanced basal and forskolin-stimulated luciferase activity. Conversely, cotransfection of AC8-luciferase with a dominant negative form of **CREB**, ACREB, reduced forskolin activation. These results support the scheme that the AC8 gene is regulated by **CREB** and may contribute to forms of **CREB** -dependent plasticity such as addiction.

L10 ANSWER 25 OF 46 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:87729 BIOSIS
DOCUMENT NUMBER: PREV200100087729
TITLE: **CREB** phosphorylation and the persistence of levodopa-induced motor response alterations in parkinsonian rats.
AUTHOR(S): Oh, J. D. [Reprint author]; Chartisathian, K.; Vaughn, C.; Chase, T. N.
CORPORATE SOURCE: NINDS-ETB, NIH, Bethesda, MD, USA
SOURCE: Society for Neuroscience Abstracts, (**2000**) Vol. 26, No. 1-2, pp. Abstract No.-278.4. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 04-09, 2000. Society for Neuroscience.
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Feb 2001
Last Updated on STN: 12 Feb 2002

AB To elucidate cellular mechanisms that underly the enduring alterations in motor response occurring with levodopa treatment of parkinsonian patients, we evaluated the time course of these changes in relation to the Ser-133 phosphorylation of striatal **CREB** in response to acute levodopa challenge in 6-hydroxydopamine (6-OHDA) animals. Three weeks of twice daily levodopa treatment induced a significant reduction in the duration of the rotational response in hemiparkinsonian rats, which lasted about five weeks after levodopa withdrawal. This shortening in response duration, resembling human wearing-off fluctuations, produced by treatment with levodopa or the D1 receptor-preferring agonist SKF 38393, but not the D2 receptor-preferring agonist quinpirole, was associated with enhanced striatal phospho-**CREB** immunoreactivity in response to acute dopaminomimetic challenge. The time course of **CREB** phosphorylation changes correlated with the time course of the changes in motor behavior following cessation of the chronic levodopa therapy. Both the change in motor response duration and degree of **CREB** phosphorylation were attenuated by **CREB anti-sense** or the PKA inhibitor Rp-cAMPS, agents that disrupt the activity of this transcriptional factor by reducing pCREB levels. The results suggest that **CREB** phosphorylation in D1 receptor expressing medium spiny neurons contributes to the persistence of motor response alterations produced by the intermittent stimulation of striatal dopaminergic receptors.

L10 ANSWER 26 OF 46 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:72787 BIOSIS
DOCUMENT NUMBER: PREV200000072787
TITLE: **Antisense**-mediated **CREB** knockdown induces hyper-reactivity to L-DOPA in a rat model of Parkinson's disease.

AUTHOR(S): Andersson, M. [Reprint author]; Cenci, M. A. [Reprint author]
CORPORATE SOURCE: Dept. Physiol. Sci., Neurobiol. Div., Wallenberg Neuroscience Centre, University of Lund, Solvegatan 17, 223 62, Lund, Sweden
SOURCE: Society for Neuroscience Abstracts, (**1999**) Vol. 25, No. 1-2, pp. 327. print.
Meeting Info.: 29th Annual Meeting of the Society for Neuroscience, Part 1. Miami Beach, Florida, USA. October 23-28, 1999. The Society for Neuroscience.
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Feb 2000
Last Updated on STN: 3 Jan 2002

L10 ANSWER 27 OF 46 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1997:528626 BIOSIS
DOCUMENT NUMBER: PREV199799827829
TITLE: **CREB antisense**, but not c-fos **antisense**, blocks NPY-induced feeding.
AUTHOR(S): Chance, W. T. [Reprint author]; Sheriff, S.; Balasubramaniam, A.
CORPORATE SOURCE: VA Med. Cent., Cincinnati, OH 45267, USA
SOURCE: Society for Neuroscience Abstracts, (**1997**) Vol. 23, No. 1-2, pp. 1345.
Meeting Info.: 27th Annual Meeting of the Society for Neuroscience. New Orleans, Louisiana, USA. October 25-30, 1997.
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Dec 1997
Last Updated on STN: 12 Dec 1997

L10 ANSWER 28 OF 46 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1996:548349 BIOSIS
DOCUMENT NUMBER: PREV199699270705
TITLE: ® Effects of acute and chronic infusions of **CREB antisense** oligonucleotides in the nucleus accumbens on cocaine self-administration.
AUTHOR(S): Self, D. W.; Spencer, J. J.; Nestler, E. J.
CORPORATE SOURCE: Div. Mol. Psychiatry, Yale Univ. Sch. Med., New Haven, CT 06513, USA
SOURCE: Society for Neuroscience Abstracts, (**1996**) Vol. 22, No. 1-3, pp. 1882.
Meeting Info.: 26th Annual Meeting of the Society for Neuroscience. Washington, D.C., USA. November 16-21, 1996.
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Dec 1996
Last Updated on STN: 13 Dec 1996

L10 ANSWER 29 OF 46 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 1995:517136 BIOSIS
DOCUMENT NUMBER: PREV199598531436
TITLE: Analysis of memory consolidation using intracerebral infusions of **antisense** oligonucleotides to the transcription factor **CREB**.
AUTHOR(S): Guzowski, J. F. [Reprint author]; Setlow, B.; Novack, G. D.; McGaugh, J. L.
CORPORATE SOURCE: Cent. Neurobiology Learning Memory, Univ. Calif., Irvine, CA 92717-3800, USA
SOURCE: Society for Neuroscience Abstracts, (**1995**) Vol. 21, No. 1-3, pp. 1947.
Meeting Info.: 25th Annual Meeting of the Society for Neuroscience. San Diego, California, USA. November 11-16, 1995.
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Dec 1995
Last Updated on STN: 6 Dec 1995

L10 ANSWER 30 OF 46 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1998:664729 SCISEARCH
THE GENUINE ARTICLE: ZZ630
TITLE: Effects of **CREB antisense** oligonucleotides on dopamine agonist-induced prodynorphin gene expression in the rat striatum
AUTHOR: Andersson M (Reprint); Cenci M A
CORPORATE SOURCE: Univ Lund, Wallenberg Neurosci Ctr, Dept Neurobiol, S-22362 Lund, Sweden
COUNTRY OF AUTHOR: Sweden
SOURCE: EUROPEAN JOURNAL OF NEUROSCIENCE, (**SEP 1998**) Vol. 10, Supp. [10], pp. 301-301. MA 11810.
ISSN: 0953-816X.
PUBLISHER: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 1
ENTRY DATE: Entered STN: 1998
Last Updated on STN: 1998

L10 ANSWER 31 OF 46 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 134:357558 CA
TITLE: Methods for treating fibroproliferative diseases
INVENTOR(S): Peterson, Theresa C.
PATENT ASSIGNEE(S): Dalhousie University, Can.
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032156	A2	20010510	WO 2000-IB1731	20001102 <--
WO 2001032156	A3	20020926		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,

LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6294350 B1 20010925 US 1999-433621 19991102 <--
PRIORITY APPLN. INFO.: US 1999-433621 A1 19991102
US 1997-870096 A2 19970605
US 1998-92317 A2 19980605

AB In accordance with the present invention, fibroproliferative disease or condition characterized by such symptoms as increased levels of c-Jun homodimers, increased heterodimerization ofc-Jun with another signaling peptide, increased levels of phosphorylated c-Jun, or increased presence of Jun kinase are treated by administering to the subject an amount of a compound effective to ameliorate one or more of the symptoms of the disease or condition, for example, an antiproliferative or antifibrotic agent. Preferred compds. for administration according to the invention are antisense c-Jun oligonucleotides and compds. that block c-Jun phosphorylation, such as pentoxifylline, or a functional derivative or metabolite thereof. Also provided by the present invention are in vitro tests for identifying whether a test compound is useful for treatment of a subject afflicted with such a disease and kits useful for conducting such assays.

L10 ANSWER 32 OF 46 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 133:291214 CA
TITLE: Antisense oligonucleotide approach to study NPY-mediated feeding signal transduction
AUTHOR(S): Sheriff, Sulaiman; Chance, William T.; Balasubramaniam, Ambikaipakan
CORPORATE SOURCE: USA
SOURCE: Methods in Molecular Biology (Totowa, New Jersey) (**2000**), 153(Neuropeptide Y Protocols), 103-114
CODEN: MMBIED; ISSN: 1064-3745
PUBLISHER: Humana Press Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors' recent in vivo studies suggest that food deprivation and intrahypothalamic NPY administration induced [32P]CRE binding activity and cAMP-responsive element binding protein (**CREB**) phosphorylation in rat hypothalamus. These intracellular signaling events may be responsible for the central regulation of eating behavior. This chapter describes the methodol. to identify the CRE-binding transcription factors mediating NPY-induced food intake in rats via an antisense oligodeoxynucleotide approach.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 33 OF 46 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 133:15266 CA
TITLE: Phosphorothioate-linked **antisense** oligonucleotides for inhibiting adenovirus p300 and **CREB** binding protein expression
INVENTOR(S): Uchida, Kiyoshi; Yokoyama, Kazunao
PATENT ASSIGNEE(S): Toa Gosei Chemical Industry Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000139464	A2	20000523	JP 1998-341086	19981113 <--
PRIORITY APPLN. INFO.:			JP 1998-341086	19981113

AB Phosphorothioate-linked **antisense** oligonucleotide complexes that are able to inhibit the expression of adenovirus E1A binding protein p300 and CBP (**CREB** binding protein) are claimed. Use of those antisense oligonucleotides as diagnostic and therapeutic agents is envisioned. Phosphorothioate-linked antisense oligonucleotides having sequences complementary to the p300 and CBP gene sequences were synthesized. Some of those oligonucleotides complexed with LipofectAMINE were effective in inhibiting the expression of those genes in mouse lung cancer F9 cells.

L10 ANSWER 34 OF 46 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	131:346847 CA
TITLE:	Membrane depolarization and cyclic AMP induced transcriptional activity of a CBP fragment in the pancreatic islet cell line HIT
AUTHOR(S):	Li, Pingfeng; Oetjen, Elke; Blume, Roland; Knepel, Willhart
CORPORATE SOURCE:	Department of Molceular Pharmacology, University of Gottingen, Gottingen, 37075, Germany
SOURCE:	Zhongguo Shengwu Huaxue Yu Fenzi Shengwu Xuebao (**1999**), 15(4), 593-596 CODEN: ZSHXF2; ISSN: 1007-7626
PUBLISHER:	Zhongguo Shengwu Huaxue Yu Fenzi Shengwu Xuebao Bianweihui
DOCUMENT TYPE:	Journal
LANGUAGE:	Chinese

AB Hormonal and elec. signals can regulate gene transcription by signal transduction pathways. The second messenger cAMP activates protein kinase A(PKA), which phosphorylates the cAMP response element(CRE)-binding protein (**CREB**)at Ser119 (in **CREB**-327, corresponding to Ser133 in **CREB**-341), leading to an increase in its transcriptional activity. Evidence suggests that both, high-potassium-induced membrane depolarization as well as cAMP initiate the influx of calcium and elevate the cytosolic Ca2+ concentration Ca2+ binds to calmodulin and activates calcium/calmodulin-dependent protein kinases which phosphorylate the transcription factor **CREB** at Ser119. Phosphorylated **CREB** recruits the coactivator **CREB** -binding protein (CBP) and thereby enhances gene transcription. Fragments of CBP have been shown to exert different effects on regulation of gene transcription. It was investigated how CBP regulates gene transcription in the insulin-producing pancreatic islet cell line HIT. A luciferase reporter gene under the control of five Gal4 binding sites was transiently transfected into HIT cells together with an expression vector for a fusion protein, containing the DNA-binding domain of the yeast transcription factor GAL4 fused to the **CREB** binding domain of CBP. Membrane depolarization and cAMP induced transcriptional activation of the CBP fragment. Both stimuli together had a synergistic effect. Stimulation by the phorbol ester TPA(12-O-tetradecanoyl phorbol-13-acetate) had no effect on CBP-mediated transactivation, indicating that a PKC-dependent pathway was not involved in CBP-dependent transcription. Another fragment of CBP that contained less amino acids and bound more strongly to **CREB** than the CBP fragment used before,showed a higher transcriptional activity. Overexpression of an expression vector for **CREB**-**antisense** diminished cAMP-stimulated, CBP-mediated transcription. These results suggest that in pancreatic islet cell gene transcription is regulated by CBP through recruitment of CBP by **CREB** in response to cAMP and membrane depolarization.

L10 ANSWER 35 OF 46 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 130:333702 CA
TITLE: **Antisense** oligonucleotides derived from gene **creb** for use as anti-leukemic agents
INVENTOR(S): Yuo, Akira; Saeki, Kumiko; Koizumi, Makoto; Fujiwara, Kousaku; Kaneko, Masakatsu
PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11103860	A2	19990420	JP 1997-265229	19970930 <--
PRIORITY APPLN. INFO.:			JP 1997-265229	19970930

AB Synthetic **antisense** phosphorothioate oligonucleotides derived from gene **creb** encoding cAMP responsive element-binding protein (**CREB**) are provided and their use as therapeutics for leukemia claimed. A clin. study using the oligonucleotides was also shown.

L10 ANSWER 36 OF 46 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 129:132065 CA
TITLE: Role of protein **CREB** in regulation of gene expression for corticotropin-releasing factor receptor and pro-opiomelanocortin in cultured rat anterior pituitary cells
AUTHOR(S): Sakai, Yoko; Horiba, Noburo; Sakai, Ken; Suda, Toshihiro
CORPORATE SOURCE: Third Dep. Intern. Med., Hirosaki Univ., Japan
SOURCE: ACTH Related Peptides (**1997**), 8, 31-36
CODEN: ARPEF9; ISSN: 1340-4512
PUBLISHER: Mitsubishi Kagaku K.K., Iyaku Jigyobu
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB With rat anterior pituitary gland cells in culture, addition of corticotropin-releasing factor (CRF) lowered (down-regulated) the expression level of CRF receptor type I mRNA. Further addition of **antisense** oligonucleotide specific to the **CREB** protein partially relieved the down-regulation of CRF receptor type I mRNA by CRF. Suppression of **CREB** expression by **antisense** oligonucleotide also lowered ACTH expression by the cells. Thus, the **CREB** protein may play a role in CRE receptor and ACTH (whose precursor is pro-opiomelanocortin) gene expression.

L10 ANSWER 37 OF 46 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 128:163346 CA
TITLE: The effect of antisense oligodeoxynucleotides on nitric oxide secretion from macrophage-like cells
AUTHOR(S): Bilecki, Wiktor; Okruszek, Andrzej; Przewlocki, Ryszard
CORPORATE SOURCE: Department of Molecular Neuropharmacology, Institute of Pharmacology, Polish Academy of Sciences, Kracow, Pol.
SOURCE: Antisense & Nucleic Acid Drug Development (**1997**), 7(6), 531-537
CODEN: ANADF5; ISSN: 1087-2906
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Nitric oxide (NO) plays an important role in cellular signaling and host

defense, and it also contributes to the deleterious effects of immune response. Until recently, the lack of specific inhibitors of various forms of nitric oxide synthase (NOS) hampered a stringent evaluation of the role played by inducible NOS (iNOS) in cell damage. The present study investigated the use of antisense oligodeoxynucleotides (AS-ODNs) to selectively inhibit the expression of iNOS. AS-ODNs (1-10 μM) inhibited, in a time-dependent and dose-dependent manner, iNOS activity in RAW 264.7 murine macrophages. Maximal inhibitory effect was >90%, and control ODNs had little or no effect on NO production Treatment with AS-ODNs decreased iNOS protein and mRNA level in studied cell, and control ODNs again were ineffective. The decreased levels of the target mRNA in AS-ODN-treated samples suggest that the AS-ODNs used act as substrates for RNase (RNase) H. Lipofection enhanced the effect of AS-ODNs on iNOS activity. However, this potentiation appears to be different from the antisense effect, in which the AS-ODNs studied were involved. Liposaccharide/interferon-γ (LPS/IFN-γ) induced iNOS, and increased NO production impaired the viability of macrophages. Treatment of RAW 264.7 cells with 10 μM AS-ODNs prevented the NO-induced lethal cell damage.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 38 OF 46 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 126:247010 CA
TITLE: Regulation of proenkephalin gene expression by transcription factors Fos and **CREB**: an **antisense** oligonucleotide approach
AUTHOR(S): Ziolkowska, Barbara; Przewlocka, Barbara; Bilecki, Wiktor; Machelska, Halina; Przewlocki, Ryszard
CORPORATE SOURCE: Inst. Pharmacol., Polish Academy Sci., Krakow, Pol.
SOURCE: Biotechnologia (**1996**), (4), 167-172
CODEN: BIECEV; ISSN: 0860-7796
PUBLISHER: Instytut Chemii Bioorganicznej PAN
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present study investigated the effects of **antisense** oligonucleotides (AS ODNs) against c-fos and **CREB** mRNA in two models of the proenkephalin (PENK) gene induction. AS ODNs to both c-fos and **CREB** mRNA markedly reduced induction of the PENK gene in the rat hippocampus in vivo during seizures produce by kainic acid (KA). In contrast, in an in vitro model of the PENK gene induction by noradrenaline and dexamethasone in C6 glioma cells, the AS ODN to c-fos was without effect whereas the AS ODN to **CREB** reduced the increase in the PENK mRNA level. The obtained results suggest that the transcription factors Fos and **CREB** may mediate induction of the PENK gene in the hippocampus, while induction of this gene in C6 glioma cells is mediated by **CREB** rather then Fos.

L10 ANSWER 39 OF 46 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 118:162310 CA
TITLE: Diversification of cyclic AMP-responsive enhancer binding proteins generated by alternative exon splicing
AUTHOR(S): Waeber, Gerard; Meyer, Terry E.; Hoeffler, James P.; Habener, Joel F.
CORPORATE SOURCE: Lab. Mol. Endocrinol., Massachusetts Gen. Hosp., Boston, MA, 02114, USA
SOURCE: Transactions of the Association of American Physicians (**1990**), 103, 28-37
CODEN: TAAPAI; ISSN: 0066-9458
DOCUMENT TYPE: Journal
LANGUAGE: English
AB PCR amplification studies in conjunction with RNase protection expts. and

sequence anal. of the human genomic cAMP-responsive enhancer-binding protein CREB327 cosmid clones clearly demonstrate that at least one of the alternative CREB327 mRNAs results from the alternative splicing of a 42-bp exon in the amino-terminal domain of the **CREB** protein-coding sequence. Interestingly, the localization of the insert is immediately upstream of the cluster of potential phosphorylation sites described previously. It is likely that this region of the **CREB** containing the multiple potential phosphorylation sites is involved in transcriptional activation function of the **CREB**.

L10 ANSWER 40 OF 46 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 117:185833 CA
TITLE: Nucleotide sequence of the bovine cyclic-AMP responsive DNA binding protein (CREB2) cDNA
AUTHOR(S): Willems, Luc; Kettmann, Richard; Chen, Gao; Portetelle, Daniel; Burny, Arsene; Derse, David
CORPORATE SOURCE: Fac. Agron., Gembloux, B5030, Belg.
SOURCE: DNA Sequence (**1991**), 1(6), 415-17
CODEN: DNSEES; ISSN: 1042-5179
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The bovine cAMP-responsive-binding protein cDNA (CREB2) was isolated from a lambda-gt11 cDNA expression library using a 32P- labeled oligonucleotide corresponding to the 21-bp enhancer sequence present in the bovine leukemia virus long terminal repeat. The deduced amino acid sequence revealed that CREB2 contains a leucine zipper structure (residue 295 to 316), a basic amino acid domain (residue 268 to 291) and several potential phosphorylation sites.

L10 ANSWER 41 OF 46 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 117:85430 CA
TITLE: Nucleotide and derived amino acid sequences of the CRE-binding proteins from rat C6 glioma and HeLa cells
AUTHOR(S): Short, Marc L.; Manohar, Chitra F.; Furtado, Manohar R.; Ghadge, Ghanashyam D.; Wolinsky, Steven M.; Thimmapaya, Bayar; Jungmann, Richard A.
CORPORATE SOURCE: Med. Sch., Northwestern Univ., Chicago, IL, 60611, USA
SOURCE: Nucleic Acids Research (**1991**), 19(15), 4290
CODEN: NARHAD; ISSN: 0305-1048
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The cAMP-responsive element-binding proteins (**CREBs**) and genes of rat C6 glioma cell and HeLa cell were sequenced.

L10 ANSWER 42 OF 46 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 116:16428 CA
TITLE: Multiple adenosine 3',5'-monophosphate response element DNA-binding proteins generated by gene diversification and alternative exon splicing
AUTHOR(S): Hoeffler, James P.; Meyer, Terry E.; Waeber, Gerard; Habener, Joel F.
CORPORATE SOURCE: Massachusetts Gen. Hosp., Harvard Med. Sch., Boston, MA, 02114, USA
SOURCE: Molecular Endocrinology (**1990**), 4(6), 920-30
CODEN: MOENEN; ISSN: 0888-8809
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The protein sequence deduced from the open reading frame of a human placental cDNA encoding a cAMP-responsive enhancer (CRE)-binding protein (**CREB**-327) has structural features characteristic of several other transcriptional transactivator proteins including jun, fos, C/EBP, myc, and CRE-BP1. Results of Southwestern anal. of nuclear exts. from several different cell lines show that there are multiple CRE-binding proteins,

which vary in size in cell lines derived from different tissues and animal species. To examine the mol. diversity of **CREB**-327 and related proteins at the nucleic acid level, labeled cDNAs from human placenta that encode 2 different CRE-binding proteins (**CREB**-317 and CRE-BP1) were used to probe Northern and Southern blots. Both probes hybridized to multiple fragments on Southern blots of genomic DNA from various species. Alternatively, when a human placental c-jun probe was hybridized to the same blot, a single fragment was detected in most cases, consistent with the intronless nature of the human c-jun gene. The **CREB**-327 probe hybridized to multiple mRNAs, derived from human placenta, ranging in size from 2-9 kilobases. In contrast, the CRE-BP1 probe identified a single 4-kilobase mRNA. Sequence analyses of several overlapping human genomic cosmid clones containing **CREB**-327 sequences in conjunction with polymerase chain reaction indicates that the **CREB**-327/341 cDNAs are composed of at least 8 or 9 exons, and analyses of human placental cDNAs provide direct evidence for at least 2 alternatively spliced exon. Analyses of mouse/hamster-human hybridoma DNAs by Southern blotting and polymerase chain reaction localizes the **CREB** -327/341 gene to human chromosome 2. The results indicate that there is a dichotomy of **CREB**-like proteins, those that are related by overall structure and DNA-binding specificity as well as those that are related by close similarities of primary sequences.

L10 ANSWER 43 OF 46 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 114:222814 CA
TITLE: A cAMP-responsive transcriptional enhancer binding protein (**CREB**), its gene cloning and uses
INVENTOR(S): Habener, Joel F.; Hoeffler, James P.
PATENT ASSIGNEE(S): General Hospital Corp., USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9005745	A1	19900531	WO 1989-US5234	19891120 <--
W: AU, JP, KR, US				
RW: AT, BE, CH, DE, ES, FR, GB, IT, LU, NL, SE				
CA 2003345	AA	19900518	CA 1989-2003345	19891120 <--
AU 9048092	A1	19900612	AU 1990-48092	19891120 <--
US 5919649	A	19990706	US 1991-684965	19910522 <--
US 6251667	B1	20010626	US 1999-252658	19990219 <--
PRIORITY APPLN. INFO.:			US 1988-272980 A2	19881118
			WO 1989-US5234 A	19891120
			US 1991-684965 A1	19910522

AB CDNA encoding **CREB** of human is cloned and sequenced, and its amino acid sequence deduced. The DNA-binding protein **CREB** is useful for the regulation of expression of a recombinant gene under control of the cAMP-responsive enhancer element (CRE). The cDNA was cloned from a human placental expression library using radioactive synthetic CRE duplex as probe. A fusion protein of **CREB** and β-galactosidase was prepared by standard methods, and binding of the fusion protein with labeled CRE probe studied. The fusion protein bound to the labeled CRE probe, and the binding was inhibited by unlabeled CRE. Also given was the similarity of the deduced protein sequence of **CREB** with c-jun protein adjacent to the leucine zipper region.

L10 ANSWER 44 OF 46 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 114:1452 CA
TITLE: Multiple cDNA clones encoding nuclear proteins that

bind to the tax-dependent enhancer of HTLV-1: all contain a leucine zipper structure and basic amino acid domain

AUTHOR(S): Yoshimura, Tadashi; Fujisawa, Junichi; Yoshida, Mitsuaki

CORPORATE SOURCE: Dep. Viral Oncol., Cancer Inst., Tokyo, 170, Japan

SOURCE: EMBO Journal (**1990**), 9(8), 2537-42
CODEN: EMJODG; ISSN: 0261-4189

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A trans-activator protein, p40tax, of human T cell leukemia virus type 1 (HTLV-1) activates its own promoter and cellular promoters of IL-2, IL-2 receptor α and GM-CSF genes. The authors isolated three cDNA clones encoding cellular proteins that bind to the p40tax-dependent enhancer of HTLV-1 by screening a λgt11 cDNA library of an HTLV-1 infected cell line. All three proteins, TREB5, TREB7, and TRE36, contained a leucine zipper structure and basic amino acid domain, which are conserved in FOS, JUN, and **CREB**, and also had multiple potential phosphorylation sites. The proteins expressed in Escherichia coli bound to the p40tax-dependent enhancer of the 21 bp sequence, but not to an inactive mutant carrying a mutation in the CRE region. In DNase I footprint anal., all three proteins protected the 21 bp sequences in the LTR; however, the patterns were not identical to each other. TREB7 and TREB36 protected all three repeats of the 21 bp, but TREB5 protected only the second repeat. TREB7 and TREB36 protected the 5' and middle portions of the 21 bp which are essential for p40tax-mediated trans-activation, whereas TREB5 and CREB1 protected a narrower part of the middle region of the second 21 bp repeat containing the CRE consensus sequence. These structural features and DNA binding properties suggest that TREB proteins are members of a **CREB** protein family and that some of them (i.e., TREB7 and TREB36) may be involved in p40tax-mediated trans-activation.

L10 ANSWER 45 OF 46 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 113:206803 CA

TITLE: Two distinct forms of active transcription factor **CREB** (cAMP response element binding protein)

AUTHOR(S): Berkowitz, Laura A.; Gilman, Michael Z.

CORPORATE SOURCE: Cold Spring Harbor Lab., Cold Spring Harbor, NY, 11724, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (**1990**), 87(14), 5258-62
CODEN: PNASA6; ISSN: 0027-8424

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Mammalian cells express 2 distinct forms of transcription factor **CREB**. Both **CREB** isoforms are expressed in many cell types and mammalian species. Both encode proteins that bind specifically to a cAMP response element. **CREB** proteins bind DNA as dimers. Both proteins impart cAMP-regulated transcriptional activity to a heterologous DNA-binding domain, showing that cAMP directly modulates the transcriptional stimulatory activity of **CREB**. The presence of multiple **CREB** isoforms with identical DNA-binding specificities but differences in the presumed regulatory domain raises the possibility that **CREB** proteins may be able to integrate distinct regulatory signals at the level of gene transcription.

L10 ANSWER 46 OF 46 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 111:227407 CA

TITLE: A cluster of phosphorylation sites on the cyclic AMP-regulated nuclear factor **CREB** predicted by its sequence

AUTHOR(S): Gonzalez, Gustavo A.; Yamamoto, Karen K.; Fischer,

Wolfgang H.; Karr, David; Menzel, Patricia; Biggs, William, III; Vale, Wylie W.; Montminy, Marc R.
CORPORATE SOURCE: Clayton Found. Lab. Pept. Biol., Salk Inst. Biol. Stud., La Jolla, CA, 92037, USA
SOURCE: Nature (London, United Kingdom) (**1989**), 337(6209), 749-52
CODEN: NATUAS; ISSN: 0028-0836
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The isolation of a cDNA clone for rat cAMP response element binding protein (**CREB**) using amino acid sequence information from purified **CREB** protein is reported. Sequence anal. of this **CREB** cDNA predicts a cluster of protein kinase A, protein kinase C, and casein kinase II consensus recognition sites near the N terminus of the protein. The proximity of these potential phosphorylation sites to one another indicates that they may interact either pos. or neg. to regulate **CREB** bioactivity.

```
=> d his

     (FILE 'HOME' ENTERED AT 18:57:51 ON 13 NOV 2005)

     FILE 'MEDLINE, BIOSIS, SCISEARCH, EMBASE, CA' ENTERED AT 19:03:54 ON 13
     NOV 2005
L1       157727 S ANTISENSE OR ANTI-SENSE OR (COMPLEM? (2N) (OLIGONUCL? OR NUCL
L2        26280 S CREB?
L3           19 S L1 (W) L2
L4          472 S L1 (P) L2
L5          247 S L1 (S) L2
L6           90 DUP REM L5 (157 DUPLICATES REMOVED)
L7           58 S L6 AND PY<=2001
L8           57 S L7 AND CREB
L9           58 S L7 AND (L1 (S) L2)
L10          46 S L8 AND (L1 (5N) L2)

=> s l1 (w) l2
L11          19 L1 (W) L2
```